An integrative view of senescence in nature

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Abstract

1. Senescence—the decline in age-specific contribution to fitness with increasing age—has been widely investigated in evolutionary ecology. A tremendous amount of detailed empirical analyses have now revealed the widespread occurrence of demographic senescence (i.e. both actuarial and reproductive senescence) and have started to identify factors (e.g. environmental conditions) that modulate its timing and intensity, both within and across species. In this special feature, we have built on this flourishing work to highlight several axes of research that would benefit from more integrative and multidisciplinary approaches.
2. Several contributions compiled in this special feature emphasize that our understanding of senescence remains taxonomically limited, mostly focused on birds and mammals, and is therefore not representative of the biological diversity displayed across the tree of life. In line with this observation, the influence of some peculiar lifestyles (e.g. involving sociality or modularity) on the evolution of senescence is yet to be deciphered.
3. Understanding of the diversity of senescence patterns across and within species and among traits will necessitate the establishment of new metrics as a golden standard to fully account for age-specific changes recorded in individuals' performance. This is illustrated with the specific case of actuarial senescence.
4. This special feature also highlights that the diversity of biological samples collected from wild plants and animals, along with accurate demographic data, is expanding. The fast development of new molecular tools now offers a unique opportunity to launch research programmes at the interface of physiology, health and ageing in non-model organisms.
5. We argue that while these different research axes constitute key avenues of investigations for the coming years, they are only the tip of the iceberg. To appreciate the full complexity of the senescence process in nature, from its evolutionary causes to its demographic consequences, we also need a better understanding of the role played by both environmental conditions and gene–environment interactions, of constraints, and of senescence, an improved assessment of the influence of individual heterogeneity, and the consideration of transgenerational effects when quantifying the fitness consequences of senescence.

KEYWORDS

ageing, demography, ecophysiology, health, life history, lifespan, scaling

Jean-Michel Gaillard and Jean-François Lemaître have contributed equally and both should be considered as first author.

1 | INTRODUCTION

Ecologists have been aware for several decades of the existence of actuarial senescence (i.e. the increase in mortality risk with age) in nature (e.g. Caughley, 1966), but they did not integrate it, and its associated evolutionary and demographic consequences, within the core of standard ecological research until the late 1990s. Since then, the field has started to flourish. Built on this increasing body of literature, a thorough synthesis of our knowledge was published 12 years ago in a *Functional Ecology* special feature entitled '*The evolutionary ecology of senescence*' (Monaghan, Charmantier, Nussey, & Ricklefs, 2008). This compilation included six contributions that pointed out:

1. The value of comparative analyses of actuarial senescence across species and the need to gather longitudinal data on health and reproductive traits (Ricklefs, 2008).
2. The value of longitudinal studies that allow separating within- from between-individual trait contribution to senescence patterns assessed at the population level (Nussey, Coulson, Festa-Bianchet, & Gaillard, 2008).
3. The role of social environmental change on the tempo of senescence in the eusocial honey bee (Münch, Amdam, & Wolschin, 2008).
4. That hormesis and metabolic syndrome can be interpreted as resulting from a mismatch between environmental conditions during early life and later in life from a refined modelling approach (Mangel, 2008).
5. That empirical tests of the quantitative genetic basis of senescence performed in the wild are broadly consistent with the evolutionary theories of senescence such as the mutation accumulation and the antagonistic pleiotropy theories (Wilson, Charmantier, & Hadfield, 2008).
6. The under-appreciated significance of the interplay between sexual selection and senescence (Bonduriansky, Maklakov, Zajitschek, & Brooks, 2008).

The common view at that time was that the process of senescence was mostly studied in humans and laboratory organisms and focused on age-specific changes in mortality risk. The contributors thus called for more studies to be performed in the wild on a broader spectrum of organisms and involving a larger range of traits. In particular, the almost complete lack of field studies on senescence in plants and the need to study reproductive senescence (i.e. a decrease in reproductive traits with age) were explicitly identified (Monaghan et al., 2008). Twelve years later, the research theme of the evolutionary ecology of senescence has moved on tremendously (see Fletcher & Selman, 2015; Shefferson, Jones, & Salguero-Gómez, 2017 for recent syntheses). From a quantitative viewpoint, a quick bibliometric analysis performed with Web of Science reveals that the ecology of senescence is a research field that has grown fast since 2008. The number of papers mentioning 'ecology' and 'senescence', 'aging' or 'ageing' more than doubled between 2008 (394 articles) and 2018 (801 articles) at a fairly constant yearly rate (+41.29 articles/year, SE = 2.66, R^2 = .96). From a qualitative viewpoint, several recommendations made by contributors of the 2008 special feature have been followed, leading to a large improvement in our understanding of the process of senescence. Nowadays, there is no more doubt that both actuarial and reproductive senescence do occur in the wild (see Jones et al., 2014; Nussey, Froy, Lemaitre, Gaillard, & Austad, 2013 for reviews of the evidence) and constitute the rule rather than the exception, at least in vertebrate species. Likewise, the process of senescence and its evolution is now generally interpreted within the conceptual framework of life-history evolution as a byproduct of the principle of energy allocation (Baudisch & Vaupel, 2012; Lemaître et al., 2015).

However, there are still obvious gaps in our understanding of the process of senescence. While demographic senescence (i.e. actuarial and reproductive senescence) has been intensively investigated thanks to the increasing availability of long-term population monitoring based on known-age individuals, empirical evidence still remains mostly limited to vertebrates. Although increasing in number, studies focusing on free-ranging species in other taxa are still rare. Moreover, while we now have fairly accurate knowledge of demographic senescence patterns in the wild, at least in mammals and birds, we know much less about age-specific changes in other biological parameters associated with physiology, life history or behaviour. In addition, whether and how age-specific changes in physiological processes (e.g. immunosenescence) interact with the environment to shape the diversity of demographic senescence patterns at both inter- and intraspecific level remains unknown. The time has come to look at senescence as an integrated dynamic evolutionary process that both shapes life-history variation within individuals, among individuals within populations, and across species, and responds to life-history variation. In that context, the 11 contributions included in this special feature *'An integrative view of senescence in nature'* can be classified into four intertwined research axes.

The first axis aims to expand our knowledge and promote research in taxa that are understudied in the field of evolutionary ecology of senescence. In particular, a special focus will be given to plants, insects and ectotherms. Roach and Smith (2020) review age-specific changes in plant traits and demonstrate a larger than expected diversity of these patterns. Although they are the taxonomic group that includes by far the greatest number of extant species, insects have been particularly overlooked in senescence studies in the wild. Zajitschek, Zajitschek, and Bonduriansky (2020) fill this knowledge gap by reviewing our current knowledge on senescence in insects and by setting the scene for future research. Lastly, Hoekstra, Schwartz, Sparkman, Miller, and Bronikowski (2020) review our current knowledge of senescence in ectotherms and emphasize that the current framework used to understand the biological basis of ageing in humans can be successfully applied to these species.

The second research axis proposes merging the process of senescence with fundamental conceptual theoretical frameworks in evolutionary ecology, namely sexual selection, pace of life and the evolution of sociality. Galipaud and Kokko (2020) review

the different ways sex and senescence interplay, with a particular focus on the rejuvenating effect of sex. Ronget and Gaillard (2020) point out the need to account for differences in the pace of life across species when analysing actuarial senescence patterns from comparative analyses. Lucas and Keller (2020) highlight the complex interplay between the evolution of sociality and lifespan, review the research on this topic performed at both inter- and intraspecific levels and then identify knowledge gaps in our current understanding of these relationships. Finally, Bernard, Compagnoni, and Salguero-Gómez (2020) provide the first general test of Finch's hypothesis that higher modularity should be associated with weaker senescence and find support for this hypothesis in plants, but not in animals.

The third research axis is intended to summarize and propose future research directions on the underlying physiological factors that shape both demographic and phenotypic senescence in the wild (and how to address them) and promote interdisciplinary research linking senescence, diseases and health in the wild (Figure 1). Regan, Froy, Walling, Moatt, and Nussey (2020) review the role of environmental variation on senescence in the wild with a special focus on dietary restriction, which has been mostly studied in controlled conditions to date. Metcalf, Roth, and Graham (2020) provide a thorough picture of the age-specific changes in immunity that occur over an individual's life course. More specifically, they highlight how selection pressures acting differently on males and females might explain the sex-specific trajectories in immune functions, which might ultimately translate into sex-specific patterns of actuarial senescence. Finally, Lemaître et al. (2020) demonstrate that the interplay between the evolution of senescence and the occurrence of carcinogenesis across and within species can be understood in the light of life-history theory and highlight how research performed within this theoretical framework can simultaneously enrich both scientific fields.

Lastly, a fourth and transversal research axis for the future of the evolutionary ecology of senescence aims to provide a synthetic view and propose future research directions on the role played by life-history trade-offs in the evolution of senescence (Figure 1), in both animals and plants. Senescence nowadays is most generally interpreted in the conceptual framework of trade-offs (i.e. a trade-off between individual performance early in life and performance late in life) under both the antagonistic pleiotropy and the disposable soma theories of ageing. Cohen, Coste, Li, Bourg, and Pavard (2020) challenge this view and point out the potentially important role of constraints in shaping the diversity of senescence patterns observed in the wild.

2 | DEFINING AND MEASURING SENESCENCE

From an evolutionary viewpoint, the process of senescence refers to a decrease in the force of natural selection with increasing age, which involves a decline in the age-specific contribution to fitness (Hamilton, 1966). By extension, for most ecologists, senescence is usually studied through the analysis of age-specific changes in biological traits directly or indirectly associated with individual fitness (Nussey et al., 2013). As actuarial senescence has been the focus of most case studies until quite recently, the metrics generally used to measure the magnitude of senescence in a focal trait correspond to the metrics traditionally used to describe actuarial senescence. This view perfectly matches what was the state of the art at the time of the previous special feature on senescence (see Monaghan et al., 2008). The Gompertz model (Gompertz, 1825)

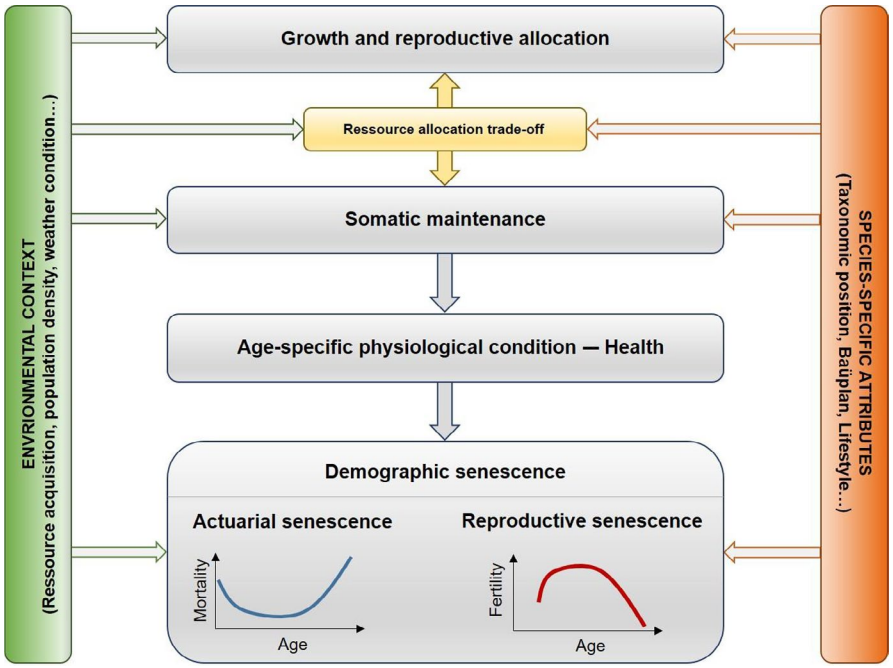

FIGURE 1 An integrative conceptual view of senescence in nature

still is at the core of empirical analyses of actuarial senescence (see Kirkwood, 2015 for an historical review) and the exponential rate of increase in mortality with age (also called *Gompertz rate*) is most often used to define the 'rate of ageing' (Ricklefs, 2008). As information on lifespan is easier to collect than age-specific mortality when studying populations in the wild, metrics of lifespan such as the maximum lifespan have often been analysed as a proxy of the 'rate of ageing', especially in comparative analyses (e.g. Møller, 2006; Reznick, Bryant, & Bashey, 2002). More than a decade ago, Monaghan et al. (2008) explicitly stated that *'a much clearer distinction needs to be drawn between life span and senescence rate'* Despite this warning and following ones (e.g. Moorad, Promislow, Flesness, & Miller, 2012), maximum lifespan is still frequently used as a proxy of the 'rate of ageing' (e.g. MacRae et al., 2015; Valcu, Dale, Griesser, Nakagawa, & Kempenaers, 2014).

In this special feature, Ronget and Gaillard (2020) provide an explicit demonstration of why maximum longevity should not be used and urge researchers to discard this metric when studying actuarial senescence. Other metrics calculated from the distribution of the ages at death (i.e. average longevity or 90% longevity) offer reliable alternatives to maximum lifespan. Recent work has also provided support to the Monaghan et al. (2008)'s statement that '*age at death by itself does not measure senescence*'. Thus, Péron, Lemaître, Ronget, Tidière, and Gaillard (2019) recently found that senescence metrics only account for less than half of the variation observed in ages at death (measured as the 90% longevity) across mammalian populations. This is because lifespan metrics calculated from the distribution of individual ages at death (but excluding maximum lifespan based on a unique individual) include two components that need to be distinguished. The first component is associated with the time-scale of the life trajectory and measures the pace of life, whereas the second one is dimensionless and describes the shape of the life trajectory (Ronget & Gaillard, 2020). By accounting for the time-scale using shape metrics, the analysis of ages at death do provide direct metrics of senescence (see also Bernard et al., 2020 in this special feature for examples of such metrics). Future analyses of senescence should thus consider a set of complementary metrics rather than be based on a unique measure, even when this latter corresponds to an explicit description of senescence.

Indeed, using the 'rate of ageing' as 'The' metric of senescence is not without problem. In life trajectories where mortality does increase exponentially with age, this pattern is only observed during a specific age range. Only few organisms, if any, display a Gompertz-type age-specific mortality from birth to the oldest age. For instance, in humans, mortality only starts to increase from 10 to 20 years of age (Gompertz, 1825), keep an exponential rate up to about 80–90 years of age, and then increases at a decreasing rate (Vaupel et al., 1998). The problem of mortality plateau can be neglected because very few organisms in the wild reach the age at which the 'rate of ageing' decelerates, leading the existence of mortality plateau to have little influence on the estimate of the strength of senescence. On the other hand, the problem of a mortality increase delayed relative to birth has to be addressed. Most analyses of senescence in the wild solved this issue by assuming that actuarial senescence starts at the age of first reproduction, as expected from our current evolutionary theory of senescence (Hamilton, 1966; Williams, 1957). However, empirical evidence of delayed actuarial senescence relative to the age at first reproduction has accumulated in recent years (e.g. Gaillard, Garratt, & Lemaître, 2017 in mammals), which questions the relevance of relying on only the 'rate of ageing'. A simple rate of linear (on a log-scale) decrease in mortality cannot provide a reliable picture of age-specific changes in mortality (and this can be easily extrapolated to any trait under study), and more thorough analyses are thus required. More flexible bathtub models such as the Siler model to describe actuarial senescence (Siler, 1979) or threshold models to describe reproductive senescence (e.g. Berman, Gaillard, & Weimerskirch, 2009) are thus required (Figure 2).

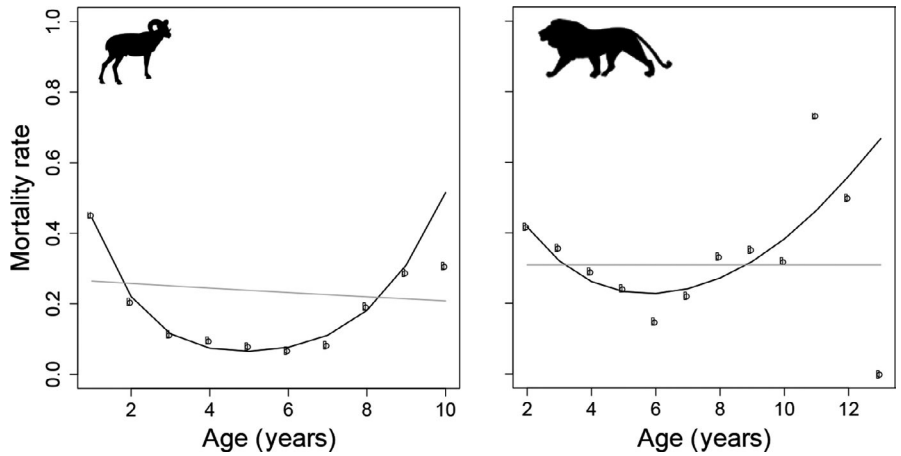

FIGURE 2 Age-specific changes in mortality rate in two mammalian species [female Soay sheep *Ovis aries* from St Kilda (Clutton-Brock & Pemberton, 2004) on the left and male lion *Panthera leo* from Serengeti National Park (Barthold, Loveridge, Macdonald, Packer, & Colchero, 2016)]. The black line corresponds to the fit of the Siler model (bathtub shape) that satisfactorily fits the observed data, whereas the grey line corresponds to the Gompertz model (exponential increase of mortality) that poorly fits the observed data. Both models are fitted from the age at first reproduction (1-year old for sheep and 2-year old for lion)

A final issue when defining and measuring senescence is the time-scale. Until recently, most, if not all, analyses of senescence were based on chronological age. However, it has become obvious that same-age individuals within a population often differ in trait values and performance, sometimes markedly. Today, the widespread use of mixture models (Hamel, Yoccoz, & Gaillard, 2017) or generalized linear mixed models (van de Pol & Verhulst, 2006) allows accounting for confounding effect of such individual heterogeneity and to obtain unbiased estimates of within-individual age-specific changes, which corresponds to the commonly used definition of senescence in evolutionary ecology. However, one may wonder whether knowing the age of a given set of individuals allows reliable prediction of their future trait trajectories. Evidence has accumulated of sudden decrease in performance one (Nussey et al., 2011) or a few (Martin & Festa-Bianchet, 2011) years before death without earlier occurrence of any decrease indicating senescence, and indicates that the age at death better predicts the life trait trajectory than chronological age (Froy et al., 2019). Time-scales based on non-chronological age can potentially offer timers that have to be explored in future studies to assess more accurately the tempo of senescence. This research field has already been tackled in human studies and a series of timers of the organism functionality (e.g. blood serum assays, auditory functioning, motor abilities, personality, life styles, Bell, 1972) have already been defined. In this special feature, Galipaud and Kokko (2020) address the question of this time-scaling issue by comparing the chronological age (called 'demographic age') and a non-chronological age corresponding to the state of the soma of an individual (called 'Abaoji-age' or 'A-age').

3 | BEYOND THE UNIVERSALITY OF THE SENESCENCE CONUNDRUM

Whether demographic senescence does occur or not in the wild has been the subject of passionate debate. During most of the 20th century, senescence was considered to be absent in nature for the simple reason that predation and harsh environmental conditions were likely to prevent any animals from growing old (Comfort, 1956; Medawar, 1952). This view has now been totally revisited. Thanks to the burst of longitudinal studies that started in the 1960s and involved the monitoring of the life trajectories of known-age individuals (Clutton-Brock & Sheldon, 2010), evidence that both survival and reproduction decline with increasing age in nature is now widespread (Nussey et al., 2013), in line with the early evolutionary prediction that senescence should be inevitable in age-structured populations (Hamilton, 1966). Therefore, the current challenge is not anymore the demonstration that senescence occurs in the wild (Brunet-Rossinni & Austad, 2006; Gaillard, Allainé, Pontier, Yoccoz, & Promislow, 1994; Nussey et al., 2008, 2013; Promislow, 1991; Ricklefs, 1998) but to answer the question: does senescence constitute an ubiquitous feature of all traits across the tree of life? Several contributions from this special feature highlight that there is no simple answer.

So far, most evidence of senescence in nature concerns avian and mammalian species, which are generally ranked at the slow side of the slow–fast continuum (Bouwhuis & Vedder, 2017; Gaillard et al., 2017; Nussey et al., 2013). This sampling bias is likely explained by the fact that most long-term field studies focused on these species (Clutton-Brock & Sheldon, 2010). The time has now come to expend the range of species where senescence is traditionally investigated in the wild to unravel its diversity (Bernard et al., 2020; Conde et al., 2019; Jones et al., 2014). This special feature puts forward three taxa that are, in that context, full of promise: insects, reptiles and plants. In their contribution, Zajitschek et al. (2020) highlight that demographic senescence has only been investigated and described in a handful of wild insect populations, although they represent the huge majority of animals on earth (May, 1986). These authors provide a clear roadmap to overcoming the methodological challenges inherent in any longitudinal monitoring of wild insects, which should thus stimulate new field investigations (Zajitschek et al., 2020). As with insects, Hoekstra et al. (2020) emphasize that our understanding of senescence in reptiles is still in its infancy. However, the diversity of demographic senescence patterns is likely to be particularly pronounced among reptiles, which range from species with unambiguous senescence to species showing negligible senescence (Hoekstra et al., 2020). Such a diversity of demographic senescence patterns appears to be even more noticeable in plants. Based on a compilation of age-specific changes in iteroparous perennials plants, Roach and Smith (2020) reveal that age-specific mortality can increase with age, stay constant or even decrease with age (i.e. negative senescence, sensu Vaupel, Baudisch, Dölling, Roach, & Gampe, 2004), as observed in the long-lived herb, *Borderea pyrenaica* (Roach & Smith, 2020). This diversity in senescence patterns is not only observed between species but also occurs within species, which emphasize the importance of considering multiple traits when it comes to study senescence. Indeed, negative actuarial senescence (i.e. decrease in mortality with age) does not preclude the occurrence of reproductive senescence, and vice-versa (Roach & Smith, 2020), which suggests that asynchronous senescence patterns might be common in plants, as recently observed in animals (Gaillard & Lemaître, 2017; Hayward et al., 2015).

Future studies in non-conventional biological models of ageing have the potential to bring new insights on the ecological and biological factors shaping this unappreciated diversity of senescence patterns (Bernard et al., 2020; Hoekstra et al., 2020; Roach & Smith, 2020; Zajitschek et al., 2020). In plants, dormancy is likely to play a key role. Indeed, by decreasing both metabolism and the physiological costs associated with harsh environmental conditions (Lesica & Crone, 2007), dormancy might delay the onset of senescence (Roach & Smith, 2020). Life styles including life stages with decreased metabolism are associated with decreased magnitude of senescence in animals (e.g. hibernation in the edible dormouse *Glis glis*, Turbill, Ruf, Smith, & Bieber, 2013). However, repeated switching from one life stage to another might, in turn, carry adverse mortality consequences (Landes et al., 2017). Taken together, these studies suggest that the relationship between repeated life stages of

reduced metabolism and senescence is likely to be complex and has to be fully deciphered. In another related contribution, Bernard et al. (2020) provide a first test of the hypothesis that modular organisms (e.g. duckweed, hydra) are more likely to escape actuarial senescence than unitary organisms. This hypothesis initially formulated by Finch (1990) posits that the anatomic barriers between modules (or sub-units) prevent the age-specific deterioration of a given set of modules to have negative consequences at the organismal level (see also Galipaud & Kokko, 2020). While the direction of the relationship between the degree of modularity and measures of pace and shape (see Section 2) are in the predicted direction in plants, the picture appears much less clear in animals, which is likely due to a lack of data to assess age dependence from published population projection matrices but also to the difficulty of ranking animals along a modularity continuum. Bernard et al. (2020) have notably ranked species according to the degree of modularity of the renal system. However, species with more modular systems (i.e. with more organs involved in ionic exchanges, partially independent lobes in reniculated kidneys such as in cetaceans) do not show any sign of prolonged lifespan or reduced senescence (Bernard et al., 2020). The study of the relationship between modularity and senescence is still at its infancy, but future research on that topic might allow identifying common eco-physiological pathways that underlie senescence in both plants and animals. Indeed, even if the ecology of senescence is an expanding research area, our current knowledge mostly relies on a relatively tiny set of species displaying broadly similar life history and life style (e.g. polygynous ungulates, passerines and seabirds, see Bouwhuis & Vedder, 2017; Gaillard et al., 2017).

Hoekstra et al. (2020)'s work identifies several factors (e.g. the evolution of protective traits such as shells or venoms) that could possibly explain why senescence seems to be generally less marked in reptiles than in birds and mammals. Among them, they notably discuss why negligible senescence could be associated with the evolution of indeterminate growth. As fecundity generally increases with size, the relative contribution to fitness of individuals growing throughout life is higher at older ages, which could lead to a selection against senescence (Jones & Vaupel, 2017; Vaupel et al., 2004). Many other factors might modulate demographic senescence. For instance, Zajitschek et al. (2020) suggest that insects could offer a suitable model to study how dispersion and migration (and their associated physiological costs) can influence senescence. They also convincingly argue that insects constitute relevant species to study the influence of sociality on senescence, a topic that constitutes the core of the contribution from Lucas and Keller (2020). Sociality can buffer environmentally driven mortality and thereby promote long lifespan, and delay and/or reduce demographic senescence through various pathways. The compilation of case studies reveals that in insects, like in birds and mammals, group size (a commonly used metric of sociality at the species level) is often positively associated with longevity (Lucas & Keller, 2020). However, this positive effect of sociality only holds in species living in large groups, which suggests that social bonds influence long-term survival only in species that display a high level of sociality. Across species, the picture is far from clear, probably because group size does not accurately reflect the level of sociality in a given species (Lucas & Keller, 2020). Previous comparisons of lifespan prospects between sociality types have revealed that eusocial species live longer than non-eusocial species in both insects (Keller & Genoud, 1997) and mammals (Healy, 2015; Williams & Shattuck, 2015). However, this lifespan benefit of sociality is only observed for the individuals holding the highest social position (i.e. queens in social insects; Lucas & Keller, 2020). Moreover, most interspecific studies compiled by Lucas and Keller (2020) have used maximum lifespan, a crude and not suitable metric of longevity (see Ronget & Gaillard, 2020, for details) that varies widely independently of the magnitude of senescence (Péron et al., 2019, see also Section 2). Although it is well established that the species position along the slow–fast continuum is a key driver of interspecific differences in senescence patterns in both birds and mammals (with fast species typically showing an earlier age at the onset of senescence and a faster rate of senescence than slow species; Jones et al., 2008), we still know only a little of the factors shaping this variability. Interspecific differences in sociality might contribute to these differences but, as rightly pointed out by Lucas and Keller (2020), studies tackling this question will need to incorporate fine-scale metrics of sociality rather than a crude measure of group size.

Importantly, studying senescence in species from under-studied taxonomic group and displaying a combination of life styles (e.g. social and modular species) that are independently associated with a decreased magnitude of senescence would allow us to widen our understanding of demographic senescence, and therefore provide new insights on population dynamics (Colchero et al., 2019). Moreover, such studies would also bring innovative insights on the physiological basis of demographic senescence and thus promote interdisciplinary research at the crossroad between biogerontology, evolutionary demography and ecology (Figure 1).

4 | TOWARDS AN INTEGRATIVE FRAMEWORK LINKING PHYSIOLOGY, HEALTH AND SENESCENCE

For obvious practical reasons, most advances in the genetic and physiological determinants of ageing have been obtained on 'classic' laboratory organisms (López-Otín, Blasco, Partridge, Serrano, & Kroemer, 2013; Partridge, 2010). Yet, field studies embedded in the 'ecology of senescence' framework are increasingly interested in the genetic and physiological basis of senescence, which has already started to create bridges between diverse research areas such as evolutionary ecology, evolutionary demography and biogerontology (Briga & Verhulst, 2015; Cohen, 2018; Fletcher & Selman, 2015; Monaghan, Eisenberg, Harrington, & Nussey, 2018; Reichard, 2016; Roach & Carey, 2014). Most research performed in the wild has focused on 'traits' (i.e. physiological functions, genetic mechanisms) that could constitute relevant mediators of life-history trade-offs (e.g. Cohen et al., 2020; Monaghan, Metcalfe, & Torres, 2009; Young, 2018). This is notably the case with oxidative stress which

has stimulated an impressive body of eco-physiological studies in the wild (e.g. Costantini, 2008) and more recently with the growing field of telomere dynamics (Monaghan et al., 2018). The relative role played by these two processes (and their interactions, see Reichert & Stier, 2017) in shaping intraspecific variation in senescence patterns in wild populations has yet to be fully deciphered (Speakman et al., 2015).

In biogerontology, the diversity of genetic and physiological manifestations of senescence observed throughout the lifespan of an organism are aggregated around well-defined (albeit inter-connected) hallmarks of ageing (e.g. loss of proteostasis, epigenetic alterations, Kennedy et al., 2014; López-Otín et al., 2013). Understanding the wide diversity of demographic senescence patterns observed across and within species would require fine-scale studies of these hallmarks in non-model organisms displaying a wide diversity of life-history strategies. While short-lived primates and companion dogs are—rightly—suggested to provide such relevant models (Kennedy et al., 2014), Hoekstra et al. (2020) demonstrate that reptiles constitute a promising taxonomic group to investigate these different hallmarks of ageing. By embracing the above-mentioned biogerontological framework, they highlight some discrepancies in the physiological manifestations of ageing between reptiles and mammalian models, which can provide new insights on the biological foundations of an extended lifespan and a slow (or delayed) senescence. If we take the accumulation of macromolecular damages as an example, dermal fibroblast cells from two snake species (garter snake *Thamnophis elegans*, and corn snake *Pantherophis guttatus*) are more resistant to cytotoxic agents than avian or mammalian fibroblasts (Alper, Bronikowski, & Harper, 2015). Similarly, social species also offer a valuable opportunity to improve our understanding of the physiological determinants of ageing, by notably comparing individuals displaying distinct social status, and thus different survival prospects (reviewed in Lucas & Keller, 2020). For instance, in 2-month old ants *Lasius niger*, the level of expression of genes involved in DNA repair is higher in long-lived queens than in short-lived workers (Lucas, Privman, & Keller, 2016). Taken together, these results emphasize that the well-established role of DNA repair mechanisms on lifespan (e.g. MacRae et al., 2015 for mammals) largely extend to non-traditional biological models of ageing.

Queens and workers also differ in immunocompetence, with queens generally having higher immunocompetence than workers (Lucas & Keller, 2020), which also emphasize the central role of immunity in shaping demographic senescence. In fact, most studies that aimed to link physiology, health and senescence in the wild have focused on immunity (e.g. Benton et al., 2018 in badgers *Meles meles*). This can be explained by the fact that, similarly to human and livestock, pathogens represent a major survival threat for animal populations in the wild (Daszak, Cunningham, & Hyatt, 2000) and also by the efficiency of the immune response, which has been repeatedly proposed as a mediator of life-history trade-offs (Sheldon & Verhulst, 1996). In this special feature, Metcalf et al. (2020) provide a critical reappraisal of the complex relationship between immunity and senescence, and of the numerous trade-offs that involve immunity all along the life course. They notably highlight the diversity of age-specific trajectories of immune performance, which likely differ between immune components (e.g. stronger senescence in the adaptive immune response than in the innate immune response, Peters, Delhey, Nakagawa, Aulsebrook, & Verhulst, 2019) or across species (see Hoekstra et al., 2020 for a discussion in reptiles). Metcalf et al. (2020) suggest the use of traits measuring the efficiency of the immune response rather than its abundance when assessing immunosenescence. They also argue that a complete understanding of the changes in immune performance over the entire life course requires a full consideration of the age-specific costs and benefits associated with a given immune response. For instance, a strong immune response to early infections might be selected for even if it is associated with an increased risk of inflammaging in late life, which itself mitigates survival prospects (Metcalf et al., 2020).

Age-specific changes in immunity can also have an impact on one major cause of death discussed in this special feature, namely cancer. In their contribution, Lemaître et al. (2020) analyse whether immunosenescence might, to some extent, explain the increase in cancer risk with advancing age. They tackle this issue at both proximate and ultimate levels by first highlighting different mechanistic pathways linking a decline in immunocompetence to cancer risk (e.g. a decline in Natural Killer T cells) and then, by demonstrating that this 'immunosenescence–cancer' association can be embedded in a life-history framework (Lemaître et al., 2020). Indeed, if as proposed, immunosenescence is partly governed by a resource-based allocation trade-off (see also Figure 1), selection for a fast growth and/or substantial allocation to reproduction (and sexual competition) during early life might increase the risk of carcinogenesis (Boddy, Kokko, Breden, Wilkinson, & Aktipis, 2015), which ultimately lead to increase demographic senescence. While this research area is still in its infancy, the increasing availability of physiological and demographic data for populations monitored in the wild with a longitudinal sampling design, coupled with the steep increase in the number of cancer cases documented in the animal kingdom (Albuquerque, Drummond do Val, Doherty, & de Magalhães, 2018), strongly suggests that such investigations will become possible to perform within a short time.

Sex differences in mortality have been documented in various species (Austad & Fischer, 2016; Marais et al., 2018) and if we look at the most studied taxonomic groups (namely mammals and birds), some general patterns can be drawn. In mammals, it is now clearly established that males overall show a higher level of adult mortality than females, while in birds this pattern tend to be reversed (Lemaître & Gaillard, 2013; Liker & Székely, 2005; Marais et al., 2018), especially when environmental conditions are limiting (Toïgo & Gaillard, 2003). However, in terms of actuarial senescence per se, the picture is more complex because there is a clear lack of consistency in both the direction and magnitude of sex differences in actuarial senescence (in terms of both onset and rate of senescence) across species (Berger et al., 2016; Carroll & Sherratt, 2017; Catchpole, Fan, Morgan, Clutton-Brock, & Coulson, 2004). Understanding the evolution

of sex-specific senescence across species is currently a key challenge in the evolutionary ecology of ageing (Maklakov & Lummaa, 2013; Marais et al., 2018; Regan & Partridge, 2013). If, for a given species, age-specific mortality patterns differ between males and females, the underlying decline in physiological performance (in a broad sense) is likely to be sex-specific as well. A complete understanding of the evolutionary roots of sex-differences in mortality risk and health trajectories requires to decipher how both natural and sexual selection have shaped distinct age-specific trajectories of physiological performance between sexes (Austad, 2006; Garratt, 2019; Morrow, 2015; Regan & Partridge, 2013). In their article, Metcalf et al. (2020) highlight different but non-mutually exclusive pathways rooted in an eco-immunology framework, which could lead to both sex-specific longevity and actuarial senescence patterns. These authors highlight that the common interpretation that a lower immune response in males is a direct consequence of a higher level of androgens is far from being supported by available studies and probably too simplistic. Immunity should most likely be sex-specific in a qualitative way. For instance, females might be more efficient at detecting pathogens while the magnitude of the response might be higher in males (Metcalf & Graham, 2018), which might have some consequences in terms of sex-specific health (i.e. females more likely to suffer from infections at late ages; Metcalf et al., 2020). Finally, both transfer of immunity across generations and pregnancy might also influence the immune response, and thus age-specific health, in a sex-specific way (Metcalf et al., 2020). Whether these sex differences in immune response might also be linked to possible differences in cancer risk (as observed in humans, Clocchiatti, Cora, Zhang, & Dotto, 2016) across species remains unknown (Lemaître et al., 2020).

5 | FUTURE DIRECTIONS

The collection of articles compiled in this special feature will likely stimulate research in the diverse array of topics related to ageing in the wild that we have succinctly highlighted above. We hope that these questions will attract both theoreticians and empiricists who work in a wide range of species, with a particular focus on species that display an unusual set of life-history traits and have been largely neglected so far. This type of approach has already proven to be successful in the past. For instance, in the concluding remarks of their introductory article, Monaghan et al. (2008) highlighted the general lack of knowledge of senescence in plants. Things have clearly changed by now (Barks & Laird, 2015; Shefferson et al., 2017), and we currently have a much more accurate picture of the diversity of senescence patterns observed in plants as well as the life-history trade-offs that govern them (see Roach & Smith, 2020). Naturally, this special feature covers only parts of the most salient challenges that face the evolutionary ecology of ageing and is largely focused on newly emerging topics. Obviously, other research areas, which are only mentioned briefly above, correspond to exciting directions for future research as well. Some specific topics can be identified from current research on ageing in the wild.

First, the organismal phenotype and genotype, its Baüplan and the environmental context it faces all set the scene of the magnitude of senescence this organism will display (Figure 1). Although it is obvious for most ecologists, the role of gene–environment interactions on senescence still remains poorly known. Thanks to impressive progress in our ability to perform genetic studies in the wild (e.g. Charruau et al., 2016 on grey wolves *Canis lupus* from the Yellowstone National Park), we can envision significant progress in that research area in the next future. More generally, the broad ecological context has most often been overlooked in biogerontology, even in studies performed in nature. However, the environment clearly matters, as nicely reported here by Regan et al. (2020). While most studies of the positive influence of dietary restriction on lifespan detected from laboratory experiments under highly controlled conditions have been generally interpreted in terms of insulin-like signalling pathways focusing on nutrient quality, Regan et al. (2020) propose instead that the complex array of outcomes so far reported rather indicates that insulin-like signalling pathways have evolved to integrate a wide range of environmental cues. Lastly, our current view of the evolution of senescence, which is mostly based on the existence of a trade-off between allocation to competing biological functions (Figure 1) such as reproduction versus survival, is a bit simplistic (Cohen et al., 2020). Performing bivariate analyses of linear trade-offs as currently done in most cases is unlikely to capture the true covariations that exist among traits, and only provide partial explanation of the existence of senescence (Cohen et al., 2020). As rightly pointed out by Cohen et al. (2020), the role of constraints inherent to the Baüplan or the life style has been overlooked in studies of senescence performed to date and future work is required to assess the relative contribution of trade-off and constraints in shaping senescence in the wild.

Second, while the current evolutionary theory of senescence assumes that biological functions should start deteriorating at the same time (e.g. Williams (1957)), empirical evidence reported so far strongly indicates that the process of senescence is asynchronous across biological functions. Whether the pattern of this asynchrony corresponds to general constraints that affect all species similarly or varies across species in relation to life-history strategies has to be investigated in future studies.

The role of individual heterogeneity corresponds to a third topic. Although a large number of studies have focused on individual heterogeneity in recent years (see Hamel, Gaillard, & Yoccoz, 2018 for a synthesis), there is still a need for a more accurate assessment of how individual heterogeneity shape senescence patterns in the wild. In particular, while individual trait differences at a given age are most often accounted for in recent analyses of senescence, differences in the shape of senescence across individuals within a population have been largely overlooked and need to be investigated.

Fourth, while age-specific data on female reproductive traits have become widespread in the literature (at least in mammals and

birds, Bouwhuis & Vedder, 2017; Gaillard et al., 1994), most comparative analyses of demographic senescence performed so far have focused on actuarial senescence (e.g. Ricklefs, 2010; Tidière et al., 2016). Likewise, the current quest for the underlying physiological mediators of demographic senescence remains largely focused on actuarial senescence and lifespan (e.g. Froy et al., 2019). However, the increasing body of evidence revealing that reproductive and actuarial senescence are, to some extent, uncoupled (Gaillard & Lemaître, 2017; Hayward et al., 2015) suggests that age-specific changes in reproduction and mortality are probably shaped by different eco-biological factors or that the relative contribution of a given factor to actuarial and reproductive senescence differs. Recently, some insightful studies have investigated how the age-specific decline in individual performance not directly linked with individual fitness (e.g. foraging behaviour, Clay, Pearmain, McGill, Manica, & Phillips, 2018; body mass, Briga, Jimeno, & Verhulst, 2019; predatory performance, McNulty et al. 2009) can have long-term consequences in terms of both late life reproductive success and lifespan. However, whether such decline in (broadly speaking) 'physiological performance' independently influences the intensity or the timing of reproductive and actuarial senescence per se remains unknown (Figure 1). Cracking this mystery across species displaying contrasted demographic tactics (see Gaillard & Yoccoz, 2003) would provide important insights on the physiological basis of age-specific contribution to fitness. In return, this will increase our understanding on how natural and sexual selection have shaped biological functions (which might thus shed light on age-specific health issues) across species. The increasing number of studies of male reproductive senescence (Gaillard & Lemaître, 2017) also suggests that future comparative analyses should be able to inform about sex differences in reproductive senescence patterns and their driving factors (e.g. Brengdahl, Kimber, Maguire-Baxter, Malacrinò, & Friberg, 2018 in fruit fly *Drosophila melanogaster*; Sparkman et al., 2017 in red wolf *Canis rufus*).

Lastly, most studies of senescence performed to date in the wild have focused on individual phenotypes and genotypes, without considering potential negative effects of parental age on offspring traits and fitness. However, understanding age-specific variation in contribution to fitness requires a holistic view of reproductive senescence that goes far beyond the commonly used age-specific decline in female reproductive rate (Lemaître & Gaillard, 2017). In that context, it becomes crucial to understand both the extent and the magnitude of the effect of parental age on offspring performance. As rightly pointed out by Galipaud and Kokko (2020), the limited reproductive value of old parents is not only caused by their limited future lifetime but also involves poor survival prospects and low reproductive success of their offspring. There is now good evidence that maternal age can have deleterious effects on juvenile survival—the so-called 'maternal effect senescence' (e.g. Tidière et al., 2018 in ruffed lemurs *Varecia rubra* and *Varecia variegata*) and even influence offspring performance in late life (e.g. offspring lifespan, Lansing, 1947). These transgenerational effects can directly affect reproductive senescence patterns such as in great tits *Parus major* where offspring born from old mothers show an earlier onset and a stronger rate of senescence in brood size (Bouwhuis, Charmantier, Verhulst, & Sheldon, 2010).

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CONFLICT OF INTEREST

No conflicts to declare.

AUTHORS' CONTRIBUTIONS

Both authors wrote the manuscript, and gave final approval for submission.

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This manuscript does not use data.

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